determination (using a FibroScan® device) at entry (D0) and 7 days after alcohol withdrawal (D7). Stiffness values were compared using non-parametric test for paired-values. We compared (i) the 10 measures performed at D0 and at D7 for each patient; (ii) the variation of the median result of all patients (using Wilcoxon test in both cases).
Results. A total of 138 patients were included in the study [median alcohol consumption: 150 g/day (range: 40–400); hepatitis C: $n = 22$ (15.9%); cirrhosis: $n = 29$ (21.0%)]. From D0 to D7, the liver stiffness decreased significantly in 61 patients (44.2%) and increased significantly in 18 (13.0%). Considering all patients, median liver stiffness value decreased from 7.25 to kPa ($P < 0.001$). The stage of fibrosis indicated by liver stiffness changed in 47 patients between D0 and D7 (decrease in 33 and increase in 14).
Conclusion. Liver stiffness decreases significantly in nearly half of alcoholic patients after only 7 days of abstinence. This result strongly suggests that non-fibrotic lesions (such as inflammatory ones) may influence liver stiffness. From a practical point of view, it also shows that variation in alcohol consumption must be taken into account for the interpretation of liver stiffness value.

O2.2

IS HISTOLOGY THE 'ADEQUATE' GOLD STANDARD TO VALIDATE THE ASSESSMENT OF ALCOHOLIC LIVER FIBROSIS BY TRANSIENT ELASTOGRAPHY (FIBROSCAN)?

S. Mueller[1], G. Millonig[1], F. Stickel[2], T. Longerich[3], P. Schirmacher[4] and H. K. Seitz[1]
[1]Salem Medical Center, Heidelberg, Germany, [2]Institute of Clinical Pathology, University of Bern, Bern, Switzerland, [3]Institute of Medical Biometry & Informatics, University of Heidelberg, Heidelberg, Germany and [4]Department of Pathology, University of Heidelberg, Heidelberg, Germany

Background. Measurement of liver stiffness (LS) by transient elastography (Fibroscan, FS) is a novel noninvasive approach to assess liver fibrosis with a high diagnostic accuracy. However, accuracy may be even higher since histology served as gold standard in all previous LS studies although its sample error may reach up to 30%. Consequently, we here determined the AUROC for FS to detect liver cirrhosis using a combination of histology and definite clinical signs of cirrhosis as obtained by ultrasound or gastroscopy in patients with alcoholic liver disease (ALD).
Method. LS was measured in 90 patients with histologically confirmed ALD. An LS of >8 kPa was considered as cut-off for F3/4 fibrosis. Patients with significant steatohepatitis (GOT > 100 U/l) were excluded since inflammation increases LS irrespective of fibrosis. We finally compared FS-results with the combination of the histological fibrosis score (Kleiner) plus additional clinical information (macronodular surface or collateral circuits in ultrasound imaging, varices in upper GI endoscopy).
Results. A total of 77 patients were scored correctly by FS using the Kleiner score as gold standard. Of 39 patients, 4 (10.2%) with histological F3/4 fibrosis had an LS of <8 kPa, but no clinical signs of liver cirrhosis. Of 51 patients, 9 (17.6%) with histological F0-2 fibrosis had an LS of >8 kPa, 2 of them had definite clinical signs of liver cirrhosis. Two more patients had an enlarged spleen (>12 cm) suggesting portal hypertension. Thus, in 8 of 90 patients (8.8%), additional clinical information was able to resolute the divergence between histology and fibroscan. AUROC for the detection of F3/4 fibrosis by FS increased from 0.923 to 0.985 when histology in combination with clinical signs of cirrhosis was used as gold standard.
Conclusion. FS results should be compared against a combination of histology and clinical information to minimize the effects of sampling error in liver biopsy. Using this as the new gold standard, FS reaches an AUROC of 0.98 in F3/F4 diagnosis.

O2.3

ROLE OF INTESTINAL PERMEABILITY AND INFLAMMATION IN THE BIOLOGICAL AND BEHAVIORAL CONTROL OF ALCOHOL-DEPENDENT SUBJECTS

S. Leclercq, P. de Timary, N. Delzenne and P. Cani
Université Catholique de Louvain, Bruxelles, Belgium

Aims. Alcohol dependence is commonly investigated in relation to modification of various neurotransmitters in brain. Our hypothesis is that the development of alcohol dependence could also involve more peripheral mechanisms and especially gut-brain interactions. Our first goal was to test whether intestinal permeability, lipopolysaccharides (LPS) and inflammatory cytokines are increased in alcohol-dependent subjects and recover after withdrawal. To explore the possible role of gut-brain axis in alcoholism, our second goal was to test correlations between the biological and the behavioral variables that are known to play a central role in alcohol dependence, such as depression, anxiety, alcohol craving and selective attention.
Methods. Forty alcohol-dependent subjects hospitalized for detoxification program were tested both at onset (T1) and at the end (T2) of withdrawal and compared for biological and behavioral markers with a control group. Participants were evaluated for gut permeability, LPS, systemic inflammation (TNFα, IL-6, IL-10, and hsCRP) and stress (Cortisol) and for depression (BDI), anxiety (STAI), alcohol craving (OCDS) and selective attention (BAWL).
Results. Intestinal permeability and LPS that were largely increased in alcohol-dependent subjects at T1 recovered completely at T2. A low-grade inflammation was observed at T1 and recovered partially after withdrawal in parallel with the psychological variables. We found that pro-inflammatory markers were positively correlated with depression and craving. The anti-inflammatory cytokine IL-10 was negatively correlated with depression and craving.
Conclusion. Leaky gut-induced inflammation is correlated to emotions and craving for alcohol. We can therefore consider that gut–brain axis may play a significant role in the development of alcoholic pathology. IL-10 could be a protective factor in relation to emotional disturbances and relapse probability. Moreover, recent animal and human studies have shown that chronic alcohol consumption altered gut microbiota. An interesting perspective would be to test pro- or prebiotics that are known to improve the composition of gut microbiota and therefore restore the gut barrier to reduce inflammation, depression and craving to help patients to remain abstinent.

O2.4

THE LOSS OF METABOLIC CONTROL ON ALCOHOL DRINKING IN HEAVILY DRINKING ALCOHOLICS

P. de Timary
Department of Adult Psychiatry and Institute of Neuroscience, Academic Hospital St Luc, UCL, Brussels, Belgium

Background. Most physiological studies of alcoholism consider ethanol as a pharmacological agent rather than a nutrient. We conducted two studies to assess potent metabolic and endocrine factors of alcohol and nutrient intake regulation in alcoholic subjects and a possible role of a disruption of energy balance for the development of alcoholism.
Methods and results. Study 1 consists of quantitative anamneses of eating and drinking habits among 97 alcoholics. The population was split around a median alcohol intake value of 12.5 kcal/kg/day. 'Low alcohol' drinking alcoholics had high BMI and fat mass (FM) and alcohol intake was compensated for by a decrease in non-alcoholic intake. 'High alcohol' drinking alcoholics had low BMI and FM and the total intake was largely above norms. In Study 2, 22 alcoholic inpatients submitted on Day 2, 5 and 16 of abstinence to diet anamneses, calorymetry and blood sampling for the measurement of biomarkers reflecting metabolism and satiety regulation were compared with 19 matched controls. We observed increased cortisol, leptin and PYY plasma levels and decreased plasma ghrelin that might explain the observed decrease in non-alcoholic intake. However, both alcoholic and non-alcoholic intake correlated positively with basal metabolism and negatively with leptin and leptin/BMI.
Conclusion. Below 12.5kcal/kg/day alcohol intake is compensated for by a decrease in nutrient intake, probably due to changes in metabolic and satiety factors. Above 12.5 kcal/kg/day alcohol intake accelerates metabolism and decreases fat mass and leptin levels, and the total intake largely exceeds norms. A dual model for regulation of energy intake in alcoholics is suggested.

O2.5

SPECIFICITY OF MACROSTRUCTURAL ABNORMALITIES IN KORSAKOFF'S SYNDROME COMPARED WITH UNCOMPLICATED ALCOHOLISM

A. L. Pitel, G. Chételat, A. P. Le Berre, B. Desgranges, F. Eustache and H. Beaunieux
Inserm U923, Caen, France

While neuropathological studies initially reported that shrinkage of the thalamic nuclei and mammillary bodies characterized Korsakoff's syndrome (KS), neuroimaging investigations revealed widespread cerebral damage including notably brain abnormalities in the frontal cortex, hippocampus and cerebellum. Reduced volume in these brain regions has also been shown in alcoholics without ostensible neurological complications (AL). The goals of the present study were therefore to identify (i) brain volume decrease related to chronic alcohol consumption and common to both AL and KS, and (ii) regions